Base Deficit and Alveolar–Arterial Gradient During Resuscitation Contribute Independently But Modestly to the Prediction of Mortality After Burn Injury

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The main determinants of mortality after burn injury that can be measured on admission include age, total burn size (% burn), and inhalation injury (INHAL). Other variables, measured during resuscitation, may provide additional information about injury severity. We assessed the utility of early arterial blood gas (ABG) data in predicting mortality after burn injury. Data were limited to samples obtained during the first 2 days after burn injury and to those obtained during high-frequency percussive ventilation. Mean values for each patient's ABG data were calculated; subsequent analysis used these derived variables. Logistic regression analysis (LRA) was used to generate a mortality predictor using burn, age (as a cubic age score, AGE), and INHAL. LRA was then repeated with the ABG variables. A total of 162 patients were included. By univariate analysis, death was associated with increased alveolar-arterial gradient ($AaDO_2$), AGE, % burn, full-thickness burn size, INHAL, and with decreased pH and base excess. LRA of % burn, AGE, INHAL, and full-thickness burn size retained the first three variables. The addition of ABG data demonstrated that mean burn excess and mean $AaDO_2$ also contributed independently to mortality. However, there was no difference in accuracy (86%) between the two equations. By Kaplan Meier analysis, $AaDO_2$ but not BE predicted earlier death in those who died. Measured during resuscitation, metabolic acidosis (ie, a base deficit) and oxygenation failure (ie, increased $AaDO_2$) contributed independently, but modestly, to ultimate mortality after burn injury. The inclusion of these variables did not improve predictive accuracy. Whether therapies targeted at these endpoints would improve outcome is unknown. (J Burn Care Res 2006;27:289–296)

It is well-established that the total burn size, age of patient, and presence of inhalation injury are independent predictors of mortality in thermally injured patients.[1] However, several authors also have noted associations between data that become available during resuscitation and outcomes to include mortality. Thus, despite fluid resuscitation that conforms to standard formulas based on burn size and weight and that results in an adequate urine output and hemodynamic response, metabolic acidosis and/or regional ischemia during burn shock may be associated with an increased incidence of systemic inflammatory response syndrome (SIRS), acute respiratory distress syndrome (ARDS), and multiple organ dysfunction syndrome (MODS).[2] Not surprisingly, these phenomena, in turn, may lead to increased mortality. These findings have caused some authors to question the safety of the established burn-resuscitation formulas and have led them to recommend more aggressive resuscitation or resuscitation directed at alternate endpoints. Although some proposed endpoints would require the use of special equipment such as gastric tonometers, clinicians often insert an arterial catheter during the initial treatment of patients with major burns, making arterial blood gas data available. Thus, the primary objective of this study was to determine whether metabolic acidosis during the first 2 days after burn, as measured by the arterial base excess (BE), is associated with increased mortality in burn

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patients, even when burn size, age, and inhalation injury are taken in to account.

A second objective was to determine whether a decrease in oxygenation during the first 2 days after burn was associated with increased mortality. Although inhalation injury increases the rate of mortality, no grading system for severity of injury has gained widespread acceptance. During resuscitation, a decrease in oxygenation (manifested by, for instance, an increase in the alveolar arterial gradient, $AaDO_2$) may be the result of inhalation injury. Even in the absence of inhalation injury, severe burns can cause ARDS.[3] Finally, fluid resuscitation, if excessive, may lead to pulmonary edema. The hypotheses evaluated in this study were that the arterial base excess and the $AaDO_2$ are independent predictors of increased mortality in thermally injured patients.

METHODS

The Brooke Army Medical Center Institutional Review Board approved this retrospective review of existing clinical data. The computerized registry of the U.S. Army Burn Center for the period 1995 to 2002 was used. Arterial blood gas (ABG) data were acquired prospectively into a personal computer. The ABG data were then linked to the registry data. In addition to ABG data, the other data extracted included total burn size, full-thickness burn size, age, sex, and survival; these data were revalidated for this study by a research nurse.

Patients with burns of any size or etiology were included if at least one ABG measurement was performed on the day of burn or the day after burn. Patients with inhalation injury were included, even in the absence of significant cutaneous injury. Patients of all ages were included. In addition, this study was limited to ABG measurements performed on patients mechanically ventilated with a high-frequency percussive ventilator, the VDR-4 (Percussionaire, Inc., Sandpoint, ID) because we have observed significant differences in indices of oxygenation and ventilation obtained in patients ventilated with the VDR-4 as compared with patients ventilated at comparable settings with conventional ventilators. This ventilator was used at this center for all patients with inhalation injury and was used by default for the majority of all other patients requiring ventilation upon admission.[4] No effort was made to exclude patients whose care was not escalated or was withdrawn at some point during their hospital stay, for example, by means of a "do not resuscitate" order.

The modified Brooke formula was used for resuscitation.[5] Inhalation injury was diagnosed by fiberoptic bronchoscopy.[6] ABGs were performed, and ventilator settings were recorded by dedicated Burn Center respiratory therapy staff. Measurements were made using a point-of-care ABG analyzer (AVL Omni, Roche Diagnostics, Indianapolis, IN) in a laboratory certified by the College of American Pathologists. ABG values were corrected for core body temperature. The BE was calculated on line by means of the Sigaard-Andersen nomogram.[7] In this report, the term "base deficit" is used to refer to those instances in which the arterial BE is less than 0. Ventilator settings were recorded into the ABG database at the time of analysis.

The mean values for all ABG data obtained during the first 2 days after burn were calculated for each patient, and these mean values were subjected to further analysis. All available ABG data were used, regardless of the number of such measurements or the exact time after burn of the measurements. SPSS version 10.1 (Chicago, IL) was used for statistical analysis. Univariate analysis used *t*- and χ^2 tests. Stepwise logistic regression (backwards likelihood ratio method) was used for multivariate analysis and to develop equations predictive of mortality. For logistic regression, age was represented as a cubic age function, age score $= -5$ age $+$ 14 age$^2/100 -$ 9 age$^3/10{,}000$. This models our observation that mortality after burn injury reaches a minimum at age 21, increases linearly thereafter, and levels off in old age.[8] For determination of model accuracy with respect to predicting mortality, a cutpoint for probability of mortality of 0.5 was used. Kaplan Meier analysis (log rank test) was used to determine the effects of mean BE and mean $AaDO_2$ on survival time. The charts of all patients dying in the burn center were reviewed, and a cause of death assigned. Data are presented as means $\pm$ standard deviation. A $P < .05$ was considered significant.

RESULTS

One hundred sixty-two patients with 539 ABG measurements met the inclusion criteria for this study and were evaluated. Epidemiologic data are presented in Table 1. The mean age of study patients was 42.3 years $\pm$ 21.0 (range, 0–93). The mean TBSA was 37.2% $\pm$ 28.1 (range, 0–99). There were six patients with smoke inhalation injury and no significant cutaneous burns. Thirty-four percent (55 patients) did not survive to hospital discharge. These nonsurvivors were significantly older and had a larger TBSA, a larger full-thickness burn size, and a greater incidence of inhalation injury than survivors. However, there was no difference in gender between survivors and nonsurvivors.

Cause of death is presented in Table 2. Infection was the leading cause of death, accounting for 47% of deaths. Failure of resuscitation accounted for 20%. We also categorized cause of death as "DNR/burns" if care was not escalated or if care was withdrawn during the

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Table 1. Comparison of surviving and nonsurviving patients

	Live (n = 107)	Die (n = 55)	*P* Value
$AaDO_2$	140.4 ± 111.4	209.7 ± 138.0	.001
Age	36.4 ± 18.6	54.6 ± 23.2	<.001
BE	−3.2 ± 3.8	−7.3 ± 4.5	<.001
% burn	26.1 ± 22.0	58.7 ± 26.1	<.001
% third-degree burn	11.1 ± 17.3	42.3 ± 31.7	<.001
HCT	45.9 ± 8.2	44.2 ± 9.5	.248
Inhalation (%)	63 (59)	43 (78)	.014
Male (%)	77 (72)	37 (67)	.536
n(ABGs)	3.0 ± 2.0	3.9 ± 2.8	.138
$PaCO_2$	29.6 ± 8.1	31.4 ± 9.6	.274
PFR	4.1 ± 1.2	3.7 ± 1.4	.093
pH	7.43 ± 0.09	7.34 ± 0.10	<.001
PIP	27.3 ± 3.6	31.9 ± 6.7	<.001
PaO_2	227.8 ± 88.4	254.8 ± 108.5	.127
Rate	12.0 ± 1.9	12.8 ± 2.7	.044

HCT, hematocrit, %; *n(ABGs)*, no. of ABGs obtained; *PFR*, PaO_2-to-FiO_2 ratio, mmHg/%; *PIP*, peak inspiratory pressure, cmH_2O; *Rate*, set ventilator rate, breaths/min.
Values are means ± SD.

resuscitation phase because of the severity of burns; this accounted for 13% of deaths. Furthermore, we classified cause of death as "DNR/terminal illness" if care was not escalated or withdrawn during the resuscitation phase because of preexisting terminal illness (eg, metastatic cancer); this accounted for 4%.

ABG and ventilator data are also presented in Table 1. Univariate analysis demonstrated that during the first 2 days after burn injury, nonsurvivors had higher mean $AaDO_2$, peak inspiratory pressure (PIP), and respiratory rate values, and lower mean pH and BE values than did survivors. Differences in the hematocrit, partial pressure of carbon dioxide ($PaCO_2$), PaO_2-to-FiO_2 ratio (PFR), and PaO_2 were not significant. Also, although more ABGs were obtained in nonsurvivors than in survivors, this difference was not significant.

Multivariate analysis was conducted in two steps. First, age (represented as the age score, as defined previously), total burn size, full-thickness burn size, and inhalation injury were evaluated. Age score, total burn size, and inhalation injury were retained in a model with an accuracy of 86% (sensitivity 84%, specificity 88%, Cox and Snell $r^2 = 0.44$). The area under the receiver operating characteristic curve (AUC ROC) was .835. In this model, probability of mortality is given by p mort = $e^k/1 + e^k$, where

$$k = -4.286 + 0.021\,(\text{agescore}) + 0.64\,(\%\text{burn}) + 0.879\,(\text{inhal}) \quad (1)$$

and agescore is the cubic age score, %burn is the total burn size, and inhal is the presence or absence of inhalation injury (1,0).

Next, ABG variables significant by univariate analysis were evaluated along with total burn size, age score, and inhalation injury. BE and $AaDO_2$ were retained, along with total burn size, age score, and inhalation injury. The accuracy of the model was unchanged at 86% (sensitivity 83%, specificity 87%, Cox and Snell $r^2 = 0.48$, AUC ROC = 0.826). In this model, probability of mortality is given by p mort = $e^k/1 + e^k$, where

$$k = -5.475 + 0.056\,(\%\text{burn}) + 0.021\,(\text{agescore}) - 0.154\,(\text{meanBE}) + 0.004\,(AaDO_2) + 0.966\,(\text{inhal}) \quad (2)$$

and meanBE is the mean arterial base excess (expressed as a positive number, such that a base deficit has a negative value).

Although accuracy was similar for the two models, incorporation of $AaDO_2$ and mean BE in the second model resulted in reclassification of a total of 13 patients (assuming a probability cut point of 0.5). For the first model, 49 patients were predicted to die; for the second model, 48 patients were predicted to die. In the second model (compared with the first), 6 patients were reclassified from predicted survival to predicted death, and 7 patients were reclassified from predicted death to predicted survival. More specifically, the new model correctly reclassified three patients to predicted survival who in fact did survive and correctly reclassified four patients to predicted death who in fact did die; however, it was at the expense of incorrect reclassification of six other patients. Thus, the net effect of the inclusion of ABG data in the second model on overall accuracy was negligible, but when applied to the 13 patients who were reclassified the new model, had a significant impact on the predicted mortality for those individuals.

An example of the output of the second model (incorporating $AaDO_2$ and mean BE) is given in Figure 1. Note in this example that whereas burn size (positively) and mean BE (negatively) both contribute independently to an increased probability of mortality, this relationship is not linear. Rather, the presence of a base deficit (e.g., BE = −8) exerts a maximal effect on increasing the risk of death for patients whose burn size is midrange. A base deficit exerts relatively less effect when burn size is small (and sur-

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Table 2. Cause of death analysis (n = 54)

	n (%)	TBSA	Age	Baux	LOS
Infection	26 (47%)	55 ± 23	51 ± 22	106 ± 25	24.0 ± 15.8
Failure of resuscitation	11 (20)	71 ± 27	52 ± 21	123 ± 27	1.4 ± 0.8
DNR/burns	7 (13)	77 ± 19	56 ± 29	133 ± 17	1.6 ± 1.6
Cardiopulmonary event	4 (7)	52 ± 16	69 ± 17	120 ± 27	5.5 ± 1.3
Hypoxia or CO at fire scene	3 (6)	30 ± 39	83 ± 14	113 ± 46	2.3 ± 1.5
DNR/terminal illness	2 (4)	65 ± 29	76 ± 15	140 ± 14	2.0 ± 0.0
Inhalation injury	1 (2)	14	23	37	10

Baux, the sum of age and TBSA; *Cardiopulmonary event*, death secondary to acute myocardial infarction, pulmonary embolus, or sudden death. *DNR/burns*, death secondary to burn shock, with a decision not to escalate care, or to withdraw care, during the resuscitation period *because of the severity of burns*; *DNR/terminal illness*, death secondary to burn shock, with a decision not to escalate care, or to withdraw care, during the resuscitation period *because of preexisting terminal illness*; *Failure of resuscitation*, death secondary to burn shock despite efforts at resuscitation; *Hypoxia or CO at fire scene*, death secondary to consequences of hypoxia or carbon monoxide poisoning, sustained at the fire scene; *Infection*, death secondary to infection and/or multiple system organ failure secondary to infection; *Inhalation injury,* death secondary to inhalation-injury-induced lung failure; *LOS*, length of stay, days; *TBSA*, total body surface area burned, percent.

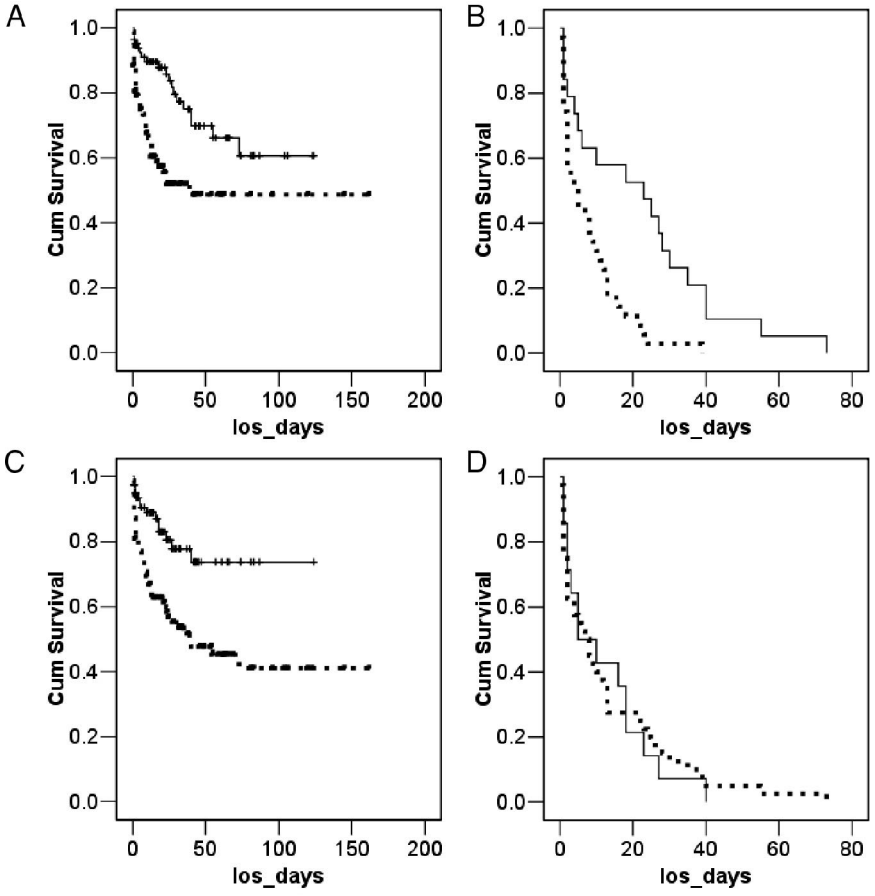

Figure 1. Kaplan-Meier analysis of the effects of mean alveolar-arterial gradient ($AaDO_2$) and mean base excess (BE) on survival time. Dotted lines represent more abnormal values (higher $AaDO_2$, lower BE). In A and B, the patients were divided into two equal groups based on the median $AaDO_2$, 125. In A, all patients in the study were included in the analysis ($P = .0012$, log rank test); whereas in B, only patients who died were included ($P = .0007$). In C and D, the patients were divided based on the median BE, −4.2. In C, patients who died were included ($P = .8926$). Thus, higher $AaDO_2$ but not lower BE predicts earlier death.

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vival is inherently likely) or when burn size is large (and survival is inherently unlikely).

Although the primary purpose of this study was to assess the effect of ABGs on survival, we also evaluated the effect of including ventilator data as well as ABG data in the logistic regression analysis. This resulted in a new model incorporating age score, %burn, and mean BE and excluding inhalation injury and $AaDO_2$, but adding mean peak inspiratory pressure (PIP):

$$k = -12.389 + 0.021\,(\text{agescore}) + 0.063\,(\%\text{burn}) - 0.166\,(\text{meanBE}) + 0.271\,(\text{meanPIP}) \quad (3)$$

The accuracy of this model was slightly improved at 88% (sensitivity 86%, specificity 89%, Cox and Snell $r^2 = 0.51$, AUC ROC = 0.939).

We speculated that abnormal mean $AaDO_2$ and BE data, measured during resuscitation, might influence not only the likelihood of death but also the time of death and/or the cause of death. We determined the effect of mean $AaDO_2$ and BE on survival time by means of Kaplan Meier analysis (Figure 2). In patients who died, a higher $AaDO_2$ predicted earlier death ($P = .0007$), whereas a lower BE did not ($P = 0.89$). Further analysis was performed to determine whether these results were confounded by total burn size, age, or frequency of inhalation injury. For those patients who died, total burn size, age, and inhalation injury were no different between the low BE and high BE groups (data not shown). However, the low and high $AaDO_2$ groups differed with respect to age only, which was unexpectedly lower in the high $AaDO_2$ group (49 vs 65 years, $P = .018$).

DISCUSSION

The principal finding in this study was that the mean arterial BE (negatively), and the mean alveolar $AaDO_2$ (positively), averaged during the first 2 days after burn, were identified as statistically significant independent predictors of the rate of mortality after burn, along with total burn size, age, and inhalation injury. Additional predictive accuracy was not obtained, however, by inclusion of the two ABG variables. These findings underscore the importance of always taking burn size, age, and inhalation injury into account when examining the relationship between physiologic data and mortality in patients with burns. Two additional caveats should be borne in mind. First, these data do not prove that interventions intended to correct acidosis or ameliorate lung injury would improve outcome; such conclusions would require prospective study. Second, caution should be used in applying mortality prediction mod-

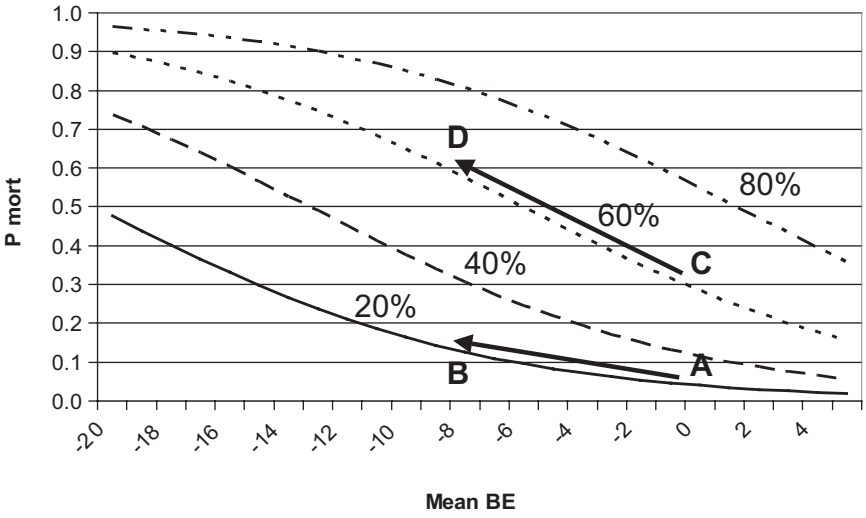

Figure 2. Visualizing the interaction between mean base excess (BE) and burn size in the mortality prediction model (equation 2) described in the text. In this example, age was held constant near the mean at 40, and alveolar-arterial gradient was held constant at the study mean (164). Each line (marked 20%, 40%, 60%, 80%) represents the relationship between mean BE and probability of mortality (P mort) for a given burn size, ranging from 20% to 80% TBSA. Note that burn size and mean BE act independently to increase mortality, but not in a linear fashion. For example, a difference in the mean BE between 0 and −8 has little effect on increased mortality risk when the burn size is relatively small at 20% (note the slope of line AB). However, a difference in the mean BE between 0 and −8 has a maximal effect on increased mortality risk when the burn size is midrange (note the slope of line CD), which suggests that a base deficit exerts the maximal effect on increased mortality risk at the midrange of burn sizes.

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els such as the one developed in this study to individual patients.

Metabolic acidosis and a decrease in the PaO_2 were recognized as consequences of thermal injury by Baxter and colleagues[9,10] in the 1950s at this Institute, soon after ABG measurement became available. Several authors have more recently analyzed the relationship between the BE (and/or serum lactate), severity of injury, and outcome in thermally injured patients. An analysis of mortality in 103 children with burns of >80% TBSA was performed by Wolf et al.[11] In that model, BE, hematocrit, and serum osmolarity were significant independent predictors of mortality (of those variables measured upon admission). This group confirmed this relationship in a subsequent prospective study.[12] Kaups et al[13] noted a relationship between a BE of −6 or less, and both larger burn size and increased postburn mortality. In an observational study of 53 burn patients, Jeng et al[14] showed that the BE often is decreased and that serum lactate levels often are increased during burn resuscitation; they suggested that these parameters should be studied as alternate indices of resuscitation adequacy. These authors subsequently reported that the initial serum lactate level and age, but not the BE or (unexpectedly) the burn size, were independent predictors of mortality after burn injury in a logistic regression model.[15] The use of continuous intra-arterial blood gas catheters then enabled these authors to document fluctuations in the BE during burn shock. They suggested that these fluctuations indicate imprecise, poorly controlled resuscitation, leading to repetitive ischemia–reperfusion cycles; future resuscitation studies may lead to closed-loop resuscitation systems, using splanchnic or cutaneous perfusion parameters as the inputs.[16]

During aggressive fluid resuscitation aimed at rapid restoration of preload and cardiac index, Holm et al[17] described a higher oxygen delivery rate and cardiac index, a lower initial serum lactate level, and faster lactate clearance in survivors than in nonsurvivors of thermal injury. Choi et al[18] calculated the mean BE for the first 24 hours after burn injury; a value less than −6 was associated with greater burn size, inhalation injury incidence, SIRS scores, and MODS scores—but not with increased mortality.[18] These findings were reproduced in a subsequent prospective study. Despite resuscitation to similar urine output endpoints (1.2–1.3 mL/kg/h), patients with mean BE less than −6 had increased SIRS and MODS scores and an increased incidence of ARDS.[2]

These findings in thermally injured patients echo the body of literature concerning the utility of the BE and/or lactate during the resuscitation of patients with nonthermal trauma. For example, Davis et al,[19] in a review of 209 trauma resuscitations, determined that a lower BE was associated with a lower mean arterial pressure and increased fluid resuscitation volume; a worsening BE during resuscitation was associated with ongoing hemorrhage in 65%. Rutherford et al[20] evaluated 3791 trauma admissions, finding that the BE independently predicted increased mortality, along with severity of injury, penetrating mechanism of injury, closed head injury, and age. The BE contributed to determining the lethal dose 25% for mechanical trauma (LD_{25}) in the following 3 scenarios 1) age <55, no head injury, and −15 BE; 2) age >55, no head injury, and −8 BE; or 3) age <55, closed head injury and −8 BE.

It often is assumed that during shock and resuscitation, changes in the lactate level will result in almost stochiometric decreases in the BE.[21] However, several studies have indicated that the lactate level during resuscitation outperforms the BE for prediction of outcome or bears little relationship to the BE.[22,23] During shock and resuscitation, changes in the BE may result from processes other than lactic acidosis. Such processes may include impairment of renal function, changes in the protein and phosphate buffer systems, and/or hyperchloremic acidosis secondary to large-volume resuscitation.[23] Lactate measure-ment was not available during the present study but, in view of these reports, we have now begun measuring lactate levels during resuscitation.

It is likely that a single BE or lactate value is less valuable than a series of values obtained over the course of, and during the day after, a resuscitation; the inability to clear lactate has been identified as a more powerful predictor of mortality than the initial value.[24–26] In the present study, with ABGs obtained at variable timepoints after injury, it was not possible to make a similar assessment, which represents a limitation of our study. Because patients had different numbers of ABGs measured at different timepoints, we took the mean value of each variable to represent the overall condition of the patient during the resuscitation period. We were concerned that more critically ill patients might undergo more frequent ABG analysis, which in turn might be more likely to detect abnormal values. It is somewhat reassuring that there was no significant difference between survivors and nonsurvivors with respect to the number of ABGs obtained during the study period.

Despite the lack of association between mean BE and survival in our study, we continue to use the BE to help guide our assessment of individual patients. Our current approach to the use of the BE during burn shock resuscitation is to consider a BE less than −6 as suggestive of significant end-organ ischemia, particularly if it persists or worsens during the course of 4 to 6 hours. Aside from a search for potentially treatable causes of metabolic acidosis—such as cyanide poisoning, missed mechanical trauma, compartment syndromes, and so forth—we be-

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lieve that patients with persistent, low BEs should be candidates for efforts to improve perfusion. However, a "risk-benefit" analysis should be performed; thus, a patient who has already received a massive resuscitation and who thus is at increased risk for abdominal compartment syndrome and other complications, is not a good candidate for even more aggressive fluid resuscitation in the face of a low BE. Rather, that patient may be a candidate for invasive monitoring, infusion of inotropes, or plasmapheresis.

Our findings also identified the $AaDO_2$ as a predictor of mortality. The pathophysiology behind this association cannot be determined from our data. However, $AaDO_2$ may relate to several factors not measured directly in this study. First, it may be reflective of the severity of smoke inhalation injury in those patients who inhaled smoke. Second, it may also indicate differences in patients' ability to compensate for smoke inhalation injury. We previously reported data from an ovine study, in which large increases in $AaDO_2$ were observed during the first 24 hours only in the group exposed to a severe dose of smoke; thus, we would speculate that a threshold effect exists for smoke inhalation injury, in which a significant deterioration in oxygenation occurs only after compensatory mechanisms are overwhelmed.[27,28] Third, acute lung injury occasionally is found as a consequence of cutaneous burns even in the absence of smoke inhalation. Acute lung injury, manifested by pulmonary edema, is uncommon during the first 2 days after burn except in the setting of massive cutaneous injury and/or massive resuscitation.[29] However, a variety of systemic processes have been shown to contribute to acute lung injury after burn; Magnotti and colleagues[30] have demonstrated the role of gut-derived lymph as one such process. Taken together, these data suggest that the lung also can be conceptualized as an end-organ during resuscitation and that impaired oxygenation during resuscitation, in patients with or without inhalation injury, may indicate a more severe injury. In our study, $AaDO_2$ but not the PFR was different between survivors and nonsurvivors. Although the PFR is easier to calculate at the bedside, the $AaDO_2$ may offer an advantage in that it incorporates information not only about oxygenation but also about ventilation. Relatedly, the inclusion of ventilator data in the logistic regression analysis resulted in a model (equation 3) that included mean PIP but excluded $AaDO_2$ and inhalation injury, suggesting that decreased compliance may be a more accurate marker of severity of lung injury than the presence of inhalation injury alone or even an increased $AaDO_2$.[31]

In this study, age was treated as a cubic age score, which incorporates the concept that, starting at birth, mortality after burn injury (controlling for burn size and inhalation injury) decreases until it reaches a nadir at age 21; it then increases and finally levels off in old age. Although not universally accepted, this concept has been validated with reference to data from other centers[32] and has been noted by others as well.[11]

A limitation of our study is the fact that complete data about time of burn, time of admission, prehospital fluid intake, and fluid resuscitation were not available for many patients and thus were not analyzed. We previously reviewed our experience with fluid resuscitation in a smaller number of burn patients.[33] In that study, the lowest BE recorded during the first 24 h after burn was an independent predictor of mortality (along with age and burn size), but not of increased fluid resuscitation volume. Others have shown that inadequate prehospital fluid resuscitation, manifested by a lower BE on admission and by a delay in establishing intravenous access, is associated with increased mortality.[11]

Another potential limitation of our study is the fact that patients with "do not resuscitate" or similar orders during the resuscitation phase were included. As can be observed (Table 2), these patients were characterized by the highest Baux Index (age plus burn size); by the highest burn size (for the DNR/burns category); and by the oldest age (for the DNR/terminal illness category). These observations suggest that the decision to forego resuscitation of these patients was appropriate and that death was highly likely for these patients. It is possible, however, that some of these patients might have lived longer if more aggressively resuscitated, which would have affected the Kaplan–Meier survival time analysis.

CONCLUSION

In a retrospective study of ABG and mechanical ventilator data obtained during the first 2 days after burn in 162 thermally injured patients treated with high-frequency percussive ventilation, we found that ultimate mortality after burn injury was predicted by logistic regression equation incorporating total burn size, age (represented as a cubic age score), inhalation injury, mean BE, and mean $AaDO_2$. However, the inclusion of the latter two terms had no effect on the overall accuracy of the equation under the conditions of this study. Nevertheless, the presence of a base deficit or of impaired oxygenation should alert the clinician to the possibility of a more severe injury than can be accounted for by burn size and inhalation injury alone. The complex pathophysiology of acid-base balance in critically ill patients, and how best to use indices such as the BE as targets of resuscitation, remain undecided issues.

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INVITED CRITIQUE

Physiologic Monitoring Proves That Sick People Are Sick

In this issue, Cancio et al[1] report that, in a review of acute burn resuscitation, two measures obtained from blood gases—alveolar-arterial oxygen difference ($AaDO_2$) and base deficit (BD)—did not improve mortality prediction when added to the universally accepted variables age, burn size, and inhalation injury. In that sense, the title of their reoirt is misleading; they could have claimed the opposite result with equal validity.

This report complements a number of other of recent studies evaluating metabolic abnormalities as predictors of outcome. In trauma patients, increased levels of lactic acid (LA) predict ongoing hemorrhage and the need to escalate resuscitation[2]; in burns, increases in the levels of BD and LA have been variously found to correlate with increasing burn size, inhalation injury, systemic inflammation, fluid requirements, and rate of mortality.[3–6]

Nonetheless, the clinical utility of these measurements remains

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unclear. Systemic acidosis is a valid marker for the unmet metabolic demands that define the shock state. However, as demonstrated, these values may not improve mortality prediction in burn patients, who already have uniquely quantifiable injuries. The authors deserve praise for their careful statistical analysis, which illuminated this point, and for thoughtfully discussing other limitations of their review. However, their study also is compromised by other considerations. First, they failed to measure LA, whichmay be a more accurate indicator of ongoing shock.[7,8] Second, they used mean values of $AaDO_2$ and BD collected during the first 2 days of treatment, so that patients with different amounts of data were compared and the most abnormal values were "diluted" as treatment proceeded. Finally, of the 55 deaths reviewed, 9 had support withdrawn, and 3 were the result of "hypoxia at the scene." Correlation of death with physiologic parameters in these patients might be predictably poor. It was surprising that $AaDO_2$ correlated more with early death because inhalation injury typically causes late deaths from pneumonia and multiple organ failure. BD, reflecting acute hypoperfusion, might have been predicted to be a better marker for early mortality.

Perhaps most importantly, no investigators have yet shown that altering fluid resuscitation to normalize these values is beneficial, or even that it can be done effectively. LA and BD often remain increased throughout a course of traditional resuscitation and decline only slowly.[6] However, it may be unavoidable; cellular dysfunction may take time to run its course. In fact, aggressive resuscitation sometimes produces transient increases in LA and BD, possibly from "wash out" of injured tissue. Attempts to resuscitate burn patients to "physiologic" goals—including normalizing oxygen delivery and LA—have not shown clear benefits but required increased fluid volumes, which may be harmful.[9] Schiller et al[10] found reduced mortality in a group of adults resuscitated to "hyperdynamic" end points, but this conflicts with the industry-wide reports of increasingly rare mortality. If traditional resuscitation is so inadequate, why is survival so good?

At present, perhaps the most we can conclude about physiologic monitoring is that it can identify patients who tolerate shock poorly and who are likely to die. This parallels experience in trauma.[11] It remains unknown whether we can change "nonresponders" into "responders" and thereby improve their prognosis. This will have to await larger trials in substantial numbers of patients. Values of BD, LA, and $AaDO_2$ might be useful in such studies in selecting patients for enrollment. Until then, it will remain unclear whether to measure—and how to manage—these parameters in acutely burned patients.

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